REMARKS

In response to the Final Official Action dated February 28, 2005, Applicant respectfully submits the present Amendment and Remarks. Pursuant to 37 CFR 1.116, reconsideration is respectfully requested.

Amendment to Claims

Claims 21 to 40 are currently pending in this application. Claims 21, 28, 29 and 32 have been amended, and new claims 36-40 have been added to the application, in order to more distinctly claim various embodiments of the invention.

Amended claims 21 and 32 have been amended to correct a typographical error by deleting the word "a". Amended claim 28 has been amended to incorporate the limitation of claim 29. Amended claim 29 has been amended to incorporate the limitation of withdrawn claim 12.

Claims 36 and 37 (depend on claims 21 and 22, respectively) have been added to incorporate the limitations of withdrawn claims 12 and 13. Claim 38 (depends on claim 29) has been added to incorporate the limitations of withdrawn claim 13. Claims 39 and 40 (depend on claims 32 and 33, respectively) have been added to incorporate the limitations of withdrawn claims 12 and 13.

Claims 21, 28, 29, 32 and 36-40 have been amended and added to clearly define the subject matter of the claimed invention. Support for these claims can be found throughout the specification, particularly in the original claims as filed. No new matter has been added. These claims do not require additional searches from the Examiner, and thus Applicant respectfully request that they be entered.

Summary of the Office Action

In the Office Action, the Examiner maintained the rejection of claims 21 to 35 under 35 U.S.C. §112, alleging that the subject matter thereof does not enable a person skilled in the art to make and use the invention commensurate in scope with the claims when the specification is only enabled for "a fusion protein comprising an anti-idiotypic anti-CEA antibody fused to a peptide consisting of SEQ ID NO: 1." The Examiner alleges that it would require undue experimentation for one skilled in the art to practice the invention as claimed since the specification discloses "only anti-idiotypic antibody 3H1 that induces anti-CEA antibody fused to a peptide consisting of SEQ ID NO: 1." The Examiner also alleges that there is insufficient guidance to the structure of the claimed peptide in the specification. Allegation that that there is "lack of guidance and working example to demonstrate that antibody comprises either light chain or heavy chain is capable of binding to any antigen" is also made in the Office Action.

The Examiner also maintained the rejection of claims 21 to 35 under 35 U.S.C. §112, alleging that the subject matter thereof does not convey that the inventor had possession of the claimed invention at the time the application was filed. The Examiner further alleges that the specification does not provide an adequate written description of the claimed invention for the same reasons in making the §112, first paragraph rejection above.

In addition, the Examiner rejected claim 28 under 35 U.S.C. §102(b), alleging that the claimed subject matter is anticipated by U.S. Patent 5,314,995 (Fell et al.). The Examiner is alleging that claim 28 is not novel in view of the cited patent.

The Examiner rejected claims 28 and 31 under 35 U.S.C. §102(b) as being anticipated by U.S. Patent 5,698,679 (Nemazee). This rejection is essentially the same as that above.

In the Official Action, the Examiner rejected claims 21 and 23 to 26 under 35 U.S.C. §103(a), alleging that the subject matter is obvious over U.S. Patent 5,314,995 (Fell et al.) or U.S. Patent 5,698,679 (Nemazee), each in view of Kang et al. and Yan et al.

The Examiner also rejected claim 32 under 35 U.S.C. §103(a), alleging that it is obvious over Rojas et al., in view of Bhattacharya-Chatterjee et al. or WO 96/20219.

Finally, the Examiner rejected claim 35 under 35 U.S.C. §103(a), alleging that it is unpatentably obvious over Rojas et al. in view of Bhattacharya-Chatterjee et al. or WO 96/20219, and further in view U.S. Patent 5,677,171.

RESPONSE

First rejection under 35 USC §112, first paragraph

As discussed above, the Examiner maintained the rejection of claims 21 to 35 under 35 U.S.C. §112, alleging that the subject matter thereof does not enable a person skilled in the art to make and use the invention commensurate in scope with the claims when the specification is only enabled for "a fusion protein comprising an anti-idiotypic anti-CEA antibody fused to a peptide consisting of SEQ ID NO: 1." Applicant respectfully traverses this rejection.

The invention as presently claimed is directed to an antigen-binding fusion protein comprising an antibody and a peptide possessing homophilic, immuno-stimulatory and/or membrane transport activities.

Applicant respectfully points out that while one of the preferred embodiments of the present invention is a fusion protein comprising an anti-idiotypic anti-CEA antibody fused to a peptide of SEQ ID NO: 1 derived from the C3d region 1217-1232, the specification clearly recites that other active peptides can be inserted into other antibodies. Specifically, column 5, lines 24-39 of U.S. Patent No. 6,238,667 (which is the parent patent of this application and which specification is incorporated into this application) further recites that peptides of the invention may have a biological activity, may comprise immunogenic epitopes, may be a hormone, ligand, etc. that may be bound to an antibody which is a full-length immunoglobulin molecule or a variable domain fragment of an antibody. See also page 12, lines 17-26 and 14, lines 1-9 of the specification of the present application.

The Office Action states that Applicant's arguments presented in the Amendment filed November 22, 2004 have been reconsidered but are not found persuasive. Applicant respectfully points out that even though the Examiner contends that the Applicant's arguments have been considered, the Examiner does not provide an explanation as to why the fourteen (14) U.S. patents recited at page 4, lines 7-20, together with the examples and procedures recited at pages 10-14,do not provide sufficient guidance to one of ordinary skill in the art to make the claimed fusion protein. Similarly, the Examiner does not provide an explanation as to why the Antibody Engineering textbook by Borrebaeck, published by Oxford University, and the Molecular Cloning laboratory manual published by Cold Spring Harbor, recited at page 4, lines 20-25 of the specification, together with the examples and procedures recited at pages 10-14, do not provide sufficient guidance to one of ordinary skill in the art to make the claimed fusion protein. These patents, textbook,

and laboratory manual are well-acknowledged literatures in the art of creating fusion proteins and are incorporated therein by reference in the specification of the present application.

The Examiner also does not provide an explanation as to why the detailed section called "Production of a Fusion Gene" recited at pages 10-14 and the examples of the specification do not provide one of ordinary skill in the art sufficient guidance to make the claimed fusion protein.

Applicant requests that the Examiner provide an explanation as to why one of ordinary skill in the art would not be able to create the claimed fusion protein from the specification, particularly at pages 4, 10-14 and the examples, as well as literatures incorporated therein.

Applicant respectfully points out that the Production of a Fusion Gene Section of the specification provides a step-to-step method of producing a fusion protein of the claimed invention. Specifically, pages 10-12 of the specification recite "As a first step in the production of a fusion protein, a blunt-end restriction site must be introduced at the desired position into the '5 end of the gene to be fused.... In order to maintain the correct reading frame, the site must...If the objective is to make a fusion protein with the complete molecule....Alternatively, if the objective is to use only a portion of the protein...."

Hence, one of ordinary skill in the art would be able to create the claimed fusion protein by the teaching and guidance of the specification of the present application, particularly at pages 4, 10-14 and the examples. Further, one of ordinary skill in the art would agree from reading the specification that the invention as presently claimed is not limited to a fusion protein with any particular peptide (or

amino acid sequence). The fusion proteins in various embodiments of the invention include a peptide possessing homophilic, immuno-stimulatory and/or membrane transport activities, where the peptide does not interfere with antigen binding. The skilled artisan can readily determine whether said peptide comprises one or more of the aforementioned activities. Moreover, Applicant respectfully submits that one of ordinary skill in the art following the teachings in the specification could practice the claimed invention with routine, if any, experimentation.

With regard to the Examiner's reliance on Stryer et al. as teaching that "the primary amino acid sequence determines the conformational [sic] of the protein," Applicant respectfully points out that the claims of the present invention are not directed to conformation of proteins.

As for Ngo et al., the Examiner is alleging that this reference teaches "the amino acid positions within a polypeptide/protein that can tolerate change ... which are critical to maintain the protein's structure/function will require guidance," Applicant respectfully submits that the application as filed, including the references cited therein, provides sufficient guidance as to the construction of fusion proteins under the invention.

As for the Examiner's reliance on Kuby et al. as teaching "antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into [a] specific conformation that contribute[s] to binding," Applicant respectfully points out that the claims of the present invention are not directed to complex three-dimensional array of scattered residues.

With regard to Examiner's reliance on Abaza et al. as teaching "a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site," Applicant respectfully points out that the invention as presently claimed is not directed to single amino acid substitutions outside of antigenic sites.

Applicant respectfully reiterates that the invention as presently claimed features fusion protein comprising (1) an antibody and (2) a peptide with homophilic, immuno-stumulatory and/or membrane transport activities, where the peptide does not interfere with antigen binding, regardless of the particulars the fusion protein conformation.

As for to the Examiner's allegation that the recitation "antibody comprises a light chain or heavy chain immunoglobulin," recited in claims 22, 27, 29, 30, 33 and 34, "[lacks] guidance and working example demonstrating that antibody comprises either light chain or heavy chain is capable of binding to any antigen," Applicant respectfully points out that lines 23-28 of page 11 of the specification recites methods used "to design a fusion gene that contains a biologically activity peptide as part of the heavy or light chain gene can use established antibody engineering protocols" as taught by Chapter 9 of the Antibody Engineering text book by Borrebaeck (which is incorporated in the specification). The Examiner has not provided any explanation as to why this teaching, together with the examples and procedures recited at pages 4 and 10-14, would not provide sufficient guidance to one of ordinary skill in the art to create the claimed fusion protein. Applicant respectfully requests that the Examiner do so.

As for the Examiner's allegation that "... it is unpredictable which peptide when fused to the antibody has which particular biological activity, in turn, would be useful for any purpose," Applicant respectfully submits that the choice of particular antibody and particular peptide comprising homophilic, immuno-stumulatory and/or membrane transport activity, is known to the skilled artisan, and the fusion protein of the invention as presently claimed is more than adequately described in the application.

Hence, Applicant respectfully submits that the specification provides the necessary guidance to apply the invention to various combinations of peptides and antibodies under the practice of the invention. The specification of the invention clearly provides an enabling disclosure for one of skill in the art to make a fusion protein using a myriad of combinations.

For at least the reasons detailed above, Applicant respectfully submits that the application as filed provides the guidance that permits one skilled in the art to make and use the invention as claimed. Applicant respectfully reminds the Examiner that the specification need not, and indeed preferably does not, exemplify all possible embodiments of the invention. Rather, the specification need only provide the necessary guidance to the skilled artisan in order to allow them to make and use the invention. Applicant respectfully submits that he has more than adequately provided such guidance in the present application.

As the specification is fully supportive of the invention as presently claimed, Applicant respectfully requests the Examiner reconsider and withdraw this rejection under 35 USC §112, first paragraph.

Second rejection under 35 USC §112, first paragraph

As discussed above, the Examiner maintained the rejection of claims 21 to 35 under 35 U.S.C. §112, alleging that the subject matter thereof does not convey that the inventor had possession of the claimed invention at the time the application was filed. Applicant respectfully traverses this rejection.

As discussed in detailed above, Applicant respectfully submits that the application as filed fully describes and exemplifies the claimed invention. Hence, there can be no doubt that Applicant had possession of the claimed invention at the time the application was filed.

Also as discussed in details above, although the Examiner stated in the Office Action that arguments made in the November 22, 2004 have been considered, no where in the Office Action does the Examiner provide explanations as to why the incorporated patents and literatures, as well as detailed explanation and examples of the specification do not provide an adequate written description of the invention. Applicant therefore respectfully requests the Examiner to provide documentary evidence support the contention that the specification of the present application and the references cited therein does not provide adequate written description for one of ordinary skill in the art would to convey that the inventor had possession of the claimed invention at the time the application was filed.

Also as discussed in detailed above, the invention as presently claimed features fusion proteins which, in various embodiments of the invention, comprise an antibody and a peptide comprising homophilic, immuno-stumulatory and/or membrane transport activity. Description of each of these embodiments of the

invention is provided in the specification as filed (including the references incorporated therein).

In the Office Action, the Examiner cited *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) and *University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 (Fed. Cir. 2004) as support for alleging that "given the lack of an additional species of antigen-binding fusion protein, peptide, antibody that binds to any cellular receptor on normal or tumor cell, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus." Applicant respectfully traverses.

With regard to the *University of California v. Eli Lilly* case, Applicant respectfully points out that in this case the Federal Circuit held that the claims of the University California patent are invalid because the specification does not comply with the written description requirement of 35 U.S.C. §112, first paragraph which is not the case in the present application. Specifically, the court held that a patent specification which includes by example a process for obtaining human insulin-encoding cDNA, and which describes the protein that the cDNA encodes, but which does not describe the structure of the claimed cDNA does no comply with the written description requirement. The court also held that the cDNA nucleotide sequence for rat insulin, as described by the patentee, did not provide a written description adequate to claim the genus of vertebrate or mammalian insulin cDNA.

The court, however, acknowledged that a description of a genus of cDNA's may be achieved by means of a recitation of a representative number of cDNA's, defined by nucleotide sequence, falling within the scope of the genus, or by a

recitation of structural features in common to the members of the genus. It is the naming of one member of such group that the court held is not a proper basis for a claim to the entire group.

In the present case, the specification does not merely naming a single peptide or species as in the case of the University of California's patent. Further, the specification of the present application sufficiently describes the fusion proteins of the claimed invention. The claim terms in the present application are not unknown biological materials that ordinary skilled in the art would easily miscomprehend instead are deemed to readily convey distinguishing information concerning the identity of the peptides as well as antibodies. Thus, as acknowledged by the court in *Lilly*, the specification of the present application provides adequate written description of a genus of the fusion protein by means of a recitation of a representative number of peptides and antibodies, defined by fusion protein, falling within the scope of the genus.

As for the *University of Rochester* case, the Federal Circuit affirmed summary judgment of invalidity for failure to comply with the written description requirement because a compound recited in the claimed methods was defined purely by functional characteristics which is different from the claims in the present application. In contrast to the claimed fusion proteins, the required compound in the *University of Rochester* patent was not disclosed in the specification and no preexisting awareness in the art of a compound exhibiting the claimed activity.

Non-steroidal anti-inflammatory drugs such as aspirin and ibuprofen function to inhibit a class of enzymes called cyclooxygenases. The University of Rochester's patent relates to the discovery of the existence and function of two distinct

cyclooxygenases, COX-1 and COX-2. COX-1 performs a beneficial function in the gastrointestinal tract. COX-2 exacerbates undesirable inflammation associated with diseases such as arthritis. Anti-inflammatory drugs which are non-steroidal and inhibit both species of cyclooxygenases and can result in both a beneficial reduction in inflammation and undesirable gastrointestinal side effects. The University of Rochester's patent is directed to a method of selectively inhibiting the COX-2 form of the enzyme by administering a non-steroidal compound that selectively inhibits activity of the COX-2 gene product. The court held that this patent neither discloses a non-steroidal compound that selectively inhibits COX-2 nor provides a suggestion as to how it could be made, and thus held it invalid for failure to comply with the written description requirement of 35 U.S.C. §112, first paragraph.

In contrast to the University of Rochester case, the specification of the present application provides adequate description of how to create the claimed fusion protein. The fusion proteins of the claimed invention include a peptide possessing homophilic, immuno-stimulatory and/or membrane transport activities, where the peptide does not interfere with antigen binding. Further, one of ordinary skill in the art can readily determine whether the claimed peptide comprises one or more of the aforementioned activities. Similarly, the present invention as presently claimed includes any particular antibody binding specificities as well as any peptides possessing one or more of the aforementioned activities so long as the peptide does not interfere with antigen binding. Thus, the claimed invention can be used in a myriad of combinations, the details of which are known to those skilled in the art. The specification clearly provides examples the necessary guidance to apply the invention to various combinations under the practice of the invention.

For at least the reasons given above, Applicant respectfully submits that the invention as presently claimed is more than adequately and definitely described in the application as originally filed. Applicant thus respectfully requests the Examiner to reconsider and withdraw this rejection under 35 USC §112, second paragraph.

First rejection under 35 USC §102 (b)

In the Office Action, the Examiner rejected claim 28 under 35 U.S.C. §102(b), alleging that the claimed subject matter is anticipated by U.S. Patent 5,314,995 (Fell et al.). The Examiner is alleging that claim 28 is not novel in view of the cited patent.

Applicant respectfully disagrees. However, in order to advance prosecution of this application, Applicant has amended claim 28 to recite:

> An antigen-binding fusion protein comprising (1) an antibody and (2) a peptide having immuno-stimulatory activity, wherein said peptide does not interfere with antigen binding, and wherein said antibody comprises a light chain or heavy chain immunoglobulin molecule and wherein said peptide is attached to the C-terminal or the N-terminal of said light chain or heavy chain immunoglobulin molecule.

The antigen-binding fusion of amended claim 28 is clearly different from the fusion protein of Fell et al. Applicant respectfully submits that the cited document fails to disclose a antigen-binding fusion protein comprising (1) an antibody and (2) a peptide having immuno-stimulatory activity, wherein said peptide does not interfere with antigen binding, and wherein said antibody comprises a light chain or heavy chain immunoglobulin molecule and wherein said peptide is attached to the C-terminal or the N-terminal of said light chain or heavy chain immunoglobulin molecule. Accordingly, Applicant respectfully requests that is rejection be withdrawn.

Second rejection under 35 USC §102 (b)

In the Office Action, the Examiner rejected claims 28 and 31 under 35 U.S.C. §102(b), alleging that the claimed subject matter is anticipated by U.S. Patent 5,698,679 (Nemazee). The Examiner is alleging that claims 28 and 31 are not novel in view of the cited patent.

Applicant respectfully disagrees. As discussed above, in order to advance prosecution of this application, Applicant has amended claims 28 and 31 to include the recitation:

> An antigen-binding fusion protein comprising (1) an antibody and (2) a peptide having immuno-stimulatory activity, wherein said peptide does not interfere with antigen binding, and wherein said antibody comprises a light chain or heavy chain immunoglobulin molecule and wherein said peptide is attached to the C-terminal or the N-terminal of said light chain or heavy chain immunoglobulin molecule.

The antigen-binding fusion of amended claims 28 and 31 are clearly different from the fusion protein of Nemazee. Again, Applicant respectfully submits that the cited document fails to disclose a antigen-binding fusion protein comprising (1) an antibody and (2) a peptide having immuno-stimulatory activity, wherein said peptide does not interfere with antigen binding, and wherein said antibody comprises a light chain or heavy chain immunoglobulin molecule and wherein said peptide is attached to the C-terminal or the N-terminal of said light chain or heavy chain immunoglobulin molecule.

Accordingly, Applicant respectfully requests that is rejection be withdrawn.

First rejection under 35 USC §103 (a)

Claims 21 and 23-26 are rejected under 35 U.S.C. §103(a) as being unpatentable over US Patent 5,314,995 (Fell et al.) or US Patent 5,698,679 (Nemazee) in view of Kang et al. and Yan et al. Applicant respectfully traverses.

As acknowledge by the Examiner, the fusion protein of Fell et al. are "useful as a method of delivering biologically active ligand molecules to the target cells or tissues and offers the advantage of decreasing systemic exposure to lymphokines and minimizing toxic effect." There is nothing in this document that teaches or suggests an anti-binding fusion protein comprising an antibody and a peptide having homophilic activity.

Also as acknowledge by the Examiner, the an antigen-binding fusion protein of Nemazee "comprising an antibody that binds specifically to a cellular receptor such as CD40 on normal cell such as APC cells and B cells fused to an immunogenic peptide such as ovalbumin." There is nothing in this document that teaches or suggests an anti-binding fusion protein comprising an antibody and a peptide having homophilic activity.

The Kang et al. document discloses T-15 antibodies. Kang et al. do not teach or suggest the use of T-15 antibodies in fusion proteins, let alone fusion proteins comprising peptides possessing homophilic activity.

Yan et al. disclose that homophilic binding provides a mechanism for amplifying the binding of monoclonal antibody to cell surface of G_{D3}. Yan et al. do not teach or suggest the use of this mechanism in making fusion proteins comprising peptides possessing homophilic activity.

Accordingly, Applicant respectfully submits it is not obvious for one of ordinary skill in the art to use the T-15 antibody of Kang et al. in the fusion protein of Fell et al. or Nemazee because there is no teaching or suggestion in the Kang et al. document to use the T-15 antibody in a fusion protein, let alone an anti-binding fusion protein comprising an antibody and a peptide having homophilic activity and has inverse hydrophathicity within the length of the peptide as recited in claims 21 and 23-26.

Similarly, it is not obvious for one of ordinary skill in the art to use the antibody of Yan et al. in the fusion protein of Fell et al. or Nemazee. As for combining the Kang et al. and the Yan et al. documents, Applicant respectfully submits that one of ordinary skill in the art would have no motivation to combine these two documents to make a fusion protein comprising a peptide possessing homophilic activity let alone a peptide having inverse hydropathicity within the length of the peptide. There is no motivation for a skilled artisan to substitute or combine the T-15 antibody of Kang et al. with the antibody of Yan et al. to make a fusion protein.

The Examiner alleges that motivation exists to combine the publications in the way she has done by merely restating the alleged teaching of these documents. The Examiner does not, however, point to specific motivation for the combination of documents stated within the four corners of the documents. Applicant respectfully submits that documents applied in combination need not only teach certain features of the claimed invention, they must also in and among themselves, provide the motivation to one of ordinary skill in the art to make the claimed combination. Applicant respectfully submits that the cited documents fail to make such a disclosure. As such, Applicant respectfully submits that this rejection of the claims is improper, and respectfully requests reconsideration and withdrawal of this rejection.

In view of the above, Applicant respectfully submits that the Office Action has not made a prima facie case of obviousness. As such, the rejection of these claims under 35 USC §103(a), discussed above, should properly be withdrawn.

Second rejection under 35 USC §103 (a)

Claim 32 is rejected under 35 U.S.C. §103(a) as being unpatentable Rojas et al. in view of Bhattacharya-Chatterjee et al. or WO 96/20219. Applicant respectfully traverses.

As acknowledge by the Examiner at page 12, first full paragraph of the Office Action, the Rojas et al. document discloses a phosphopeptide fused with a peptide, instead of an antibody fused with a peptide. Thus, this reference does not teach or suggests a fusion protein comprising an antibody and a peptide having membrane transport activity, wherein the peptide does not interfere with an antigen binding as recited in claim 32 of the present invention.

Also as acknowledged by the Examiner at page 12 of the Office Action, the Bhattacharya-Chatterjee et al. document discloses "an anti-idiotype antibody such as 3H1 that elicits the production of anti-CEA antibody that binds specifically to carcinoembryonic antigen (CEA) on normal and tumor cell in colon carcinoma. This document neither teaches nor suggests an antibody fused with a peptide in a fusion protein, let alone a fusion protein comprising an antibody and a peptide having membrane transport activity.

As for WO 96/20219, this document discloses a pharmaceutical composition comprising an anti-idiotype antibody and a pharmaceutically acceptable excipient and/or adjuvant for eliciting immune response with advanced CEA associated disease. There is nothing in this document that teaches or suggests an antibody

fused with a peptide in a fusion protein, let alone a fusion protein comprising an antibody and a peptide having membrane transport activity.

Applicant respectfully submits that there is no motivation for one of ordinary skill in the art to substitute the antibody of Bhattacharya-Chatterjee et al. with the phosphopeptide of Rojas et al to make a fusion protein comprising an antibody and a peptide having membrane transport activity as recited in claim 32.

Similarly, there is no motivation for one of ordinary skill in the art to substitute the antibody of WO 96/20219 with the phosphopeptide of Rojas et al to make a fusion protein comprising an antibody and a peptide having membrane transport activity as recited in claim 32.

Thus, one of ordinary skill in the art would have no motivation to combine the above cited documents to make an antigen-binding fusion protein comprising an antibody and a peptide having membrane transport activity.

The Examiner alleges a motivation to combine the disclosure of the references by again merely reiterating the alleged teachings of the cited documents. The Examiner does not point to any teaching or suggestion disclosed in any of the documents themselves that would motivate one of ordinary skill in the art to the claimed combination of the invention. Applicant respectfully submits that it is not enough that the cited documents may individually mention one of various features of the claimed invention. Rather, the documents must also provide the motivation for one of ordinary skill in the art to combine their disclosures. Applicant respectfully submits that the cited documents fail to provide such a motivation for the invention as presently claimed in this application.

Moreover, Applicant respectfully submits that the Examiner is "picking and choosing" pieces of the cited documents in fashioning this rejection. As such, the Examiner appears to be making this rejection under 35 USC §103(a) with the benefit of hindsight, after reading the disclosure of the instant application. Such a reliance upon hindsight, after perusing Applicant's disclosure, is "impermissible." For this reason also, this (and the previous) rejection of the claims under 35 USC §103(a) should be withdrawn. Reconsideration is respectfully requested.

In view of the above, Applicant respectfully submits that the Office Action has not made a prima facie case of obviousness. As such, the rejection of these claims under 35 USC §103(a), discussed above, should properly be withdrawn.

Third rejection under 35 USC §103 (a)

Claim 35 is rejected under 35 U.S.C. §103(a) as being unpatentable Rojas et al. in view of Bhattacharya-Chatterjee et al. or WO 96/20219, and further in view of U.S. Patent No. 5,676,171 (Hudziak et al.). Applicant respectfully traverses.

The disclosures of the Rojas et al., Bhattacharya-Chatterjee et al., and WO 96/20219 documents are discussed in detail above.

With regard to the Hudziak et al. document, this document merely discloses that a particular antibody, i.e., 3E8 binding to a membrane-spanning receptor (HERE2) is able to inhibit tumor growth. This document makes no mention whatsoever of fusion proteins comprising an antibody and a peptide having membrane transport activity.

Claim 35 depends on claim 32 and recites:

> The antigen-binding fusion protein of claim 32, wherein said antibody is specific for a cellular receptor on a normal cell or on a tumor cell.

As discussed above, there is no motivation for one of ordinary skill in the art to substitute the antibody of Bhattacharya-Chatterjee et al. or WO 96/20219 with the phosphopeptide of Rojas et al to make a fusion protein comprising an antibody and a peptide having membrane transport activity as recited in claim 32.

Therefore, there would also be no motivation for one of ordinary skill in the art to substitute the 3E8 antibody of Hudziak with the phosphopeptide of Rojas et al. to make a fusion protein comprising an antibody and a peptide having membrane transport activity.

In view of the above, Applicant respectfully submits that the Office Action has not made a prima facie case of obviousness. As such, the rejection of these claims under 35 USC §103(a), discussed above, should properly be withdrawn.

CONCLUSION

In light of the foregoing amendments and remarks, Applicant respectfully submits that the application is now in condition for allowance. Should any minor matter remain, or should the Examiner feel that an interview would expedite the prosecution of this application, the Examiner is invited to call the undersigned at his convenience.

To the extent necessary, Applicant petitions for an extension of time under 37 CFR 1.136. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to the Antonelli, Terry, Stout & Kraus, LLP Deposit Account No. 01-2135 (Docket No. 411.35629PC2), and please credit any excess fees to such Deposit Account.

Respectfully submitted,

ANTONELLI, TERRY, STOUT & KRAUS, LLP

By _____
Jessica H. Tran Bui
Reg. No. 40,846

JHB/AES

1300 North Seventeenth Street, Suite 1800
Arlington, Virginia 22209
Telephone: (703) 312-6600
Facsimile: (703) 312-6666